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HARRIET M. STRIMPEL, D. Phil.
New England Biolabs, Inc.
240 COUNTY ROAD
IPSWICH, MA 01938-2723

EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

STRIMPEL@NEB.COM
Goldberg@neb.com
wermuth@neb.com

Office Action Summary	Application No.	Applicant(s)	
	10/562,183	ZHANG ET AL.	
	Examiner	Art Unit	
	GARY W. COUNTS	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 14-22* is/are pending in the application.

4a) Of the above claim(s) *18-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Applicant's amendment and response filed 06/10/09 is acknowledged and has been entered. Currently claims 1-11 and 14-22 are pending with claims 18-22 being withdrawn as being directed to a non-elected invention. Claims 1-11 and 14-17 are under examination.

Withdrawn Rejections

All rejections of claims not reiterated herein, have been withdrawn.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1, 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hashimoto et al (Expression and Characterization of the Chitin-Binding domain of Chitinase A1 from Bacillus circulans WL-12, Journal of Bacteriology, June 2000, p. 3045-3054) in view Chong et al (Gene 192, (1997) 271-281 and further in view of Novokhatny (Protein Science (1997), 6:141-146).

Hashimoto et al disclose a method of detecting chitin in a sample. Hashimoto et al disclose contacting a reagent of chitin-binding domain with a sample containing chitin. The chitin-binding domain is $CHBD_{ChiA1}$ (p. 3047, p. 3048, p. 3051 & Figs. 1-3. Hashimoto et al disclose detecting the binding between the chitin-binding domain and the chitin. Hashimoto et al teach that this chitin-binding domain bound only to chitin and that no significant binding to cellulose or other polysaccharides was detected (p. 3051, 2nd col). Hashimoto et al provide that the chitin-binding domain was obtained from Chitinase a1 from Bacillus circulans (abstract, p. 3045).

With respect to claim 9 as indicated by applicant on page 10 of the specification, chitinase A1 contains CBD that belongs to CBM12. Thus, it is inherent that the CBD of Hosimoto et al has a carbohydrate-binding module corresponding to CBM12.

Hashimoto et al differs from the instant invention in failing to teach the chitin-binding domain is fused to a maltose-binding domain.

Chong et al teach that it is known in the art to construct fusion proteins comprising CBD fused to maltose binding protein.

Novokhatny discloses that it is well known in the art to use maltose binding protein as a carrier protein for the production of recombinant fusion proteins in E-Coli. Novokhatny teaches that the presence of maltose binding protein facilitates purification of a target protein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce and incorporate a CBD-MBP fusion protein as suggested by Chong and Novokhatny for the method of Hashimoto et al because Hashimoto et al specifically taught that the CBD can be produced in E-Coli and Chong showed that it is well known in the art to fuse CBD-MBP and because Novokhatny taught that the incorporation of a carrier protein such as maltose binding protein provides for purification of the target protein.

4. Claims 2, 3 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hashimoto et al in view of Chong et al and Novokhatny et al as applied to claims 1, 9 and 11 above, and further in view of Gray et al (US 6,399,571).

See above for the teachings of Hashimoto et al., Chong et al., and Novokhatny et al.

Hashimoto et al., Chong et al., and Novokhatny et al. differ from the instant invention in failing to specifically teach that the chitin-binding domain comprises a reporter and also fail to teach an antibody to chitin-binding domain.

Gray et al teach that it is known in the art to label chitin-binding domains with a reporter to detect chitin in a sample (col 7, lines 45-63). Gray et al also teach the use of

labeled antibodies that specifically bind to chitin-binding domains for detection of chitin-binding domain (col 6). Gray et al discloses that the reporter can be a radioisotope, fluorophore or enzyme (col 7).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a reporter such as taught by Gray et al into the modified method and chitin binding domain of Hashimoto, Chong, and Novokhatny because Hashimoto et al taught that the chitin binding domain can be used in binding assays to determine chitin in a sample and Gray et al taught that it is conventional in the art to label chitin-binding domains to provide for reagents to detect chitin in a sample. It would have also been obvious to one of ordinary skill in the art at the time the invention was made to incorporate chitin-binding domain antibodies as taught by Gray et al into the modified method of Hashimoto et al, Chong, and Novokhatny because Gray et al taught that it is conventional in the art to utilize chitin antibodies in methods for detecting chitin in a sample.

5. Claims 4 and 5 are rejected are under 35 U.S.C. 103(a) as being unpatentable over Hashimoto et al in view of Chong et al and Novokhatny et al as applied to claims 1, 9 and 11 above, and further in view of Tuse et al (WO 92/17786).

See above for the teachings of Hashimoto et al., Chong et al., and Novokhatny et al.

Hashimoto et al., Chong et al., and Novokhatny et al. differ from the instant invention in failing to teach the sample is an animal or plant fluid.

Tuse et al disclose methods of detecting chitin in samples. Tuse et al disclose that the sample can be mammalian and plant fluid, tissues or water (p. 5 and p.9).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a sample such as taught by Tuse et al into the modified method of Hashimoto et al, Chong, and Novokhatny because Tuse et al taught applications of his samples for detection of the presence of chitin.

6. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hashimoto et al in view of Chong et al and Novokhatny et al as applied to claims 1, 9 and 11 above, and further in view of Harman et al (US 6,251,390).

See above for the teachings of Hashimoto et al., Chong et al., and Novokhatny et al.

Hashimoto et al., Chong et al., and Novokhatny et al. differ from the instant invention in failing to teach bleaching the sample.

Harman et al disclose that it is known in the art to bleach a sample of chitin which provides for purification of the chitin (col 3, lines 34-51).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to bleach the sample of Hashimoto et al as suggested by Harman because Haman et al taught that it is known in the art to bleach samples of chitin in order to provide for purification of the chitin.

7. Claims 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hashimoto et al., in view of Chong et al., Novokhatny et al and Gray et al as applied to claims 1-3, 6-9 and 11 above, and further in view of Tuse et al and Foster et al.

See above for the teachings of Hashimoto et al., Chong et al., Novokhatny et al and Gray et al.

Hashimoto et al., Chong et al., Novokhatny et al and Gray et al., differ from the instant invention in failing to teach the components packaged into a kit and also fails to teach instructions and an immobilized CBD reagent.

Tuse et al teaches methods and kits for detecting chitin. Tuse et al disclose chitinase reagents which specifically bind to chitin (p. 4). Tuse et al disclose that a chitin binding domain can be immobilized to a solid support and used to capture chitin and subsequently detected to determine the chitin. Tuse et al teach that these methods provide for the advantage of detecting chitin in samples of all types of biological fluids and tissues and also provide the advantage of an efficient, economical, clinical laboratory assay for the rapid diagnosis of fungal inflections in patients.

Foster et al disclose instructions (packaging material) packaged in a kit for using the kit (col 15).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the immobilization reagents for chitin binding domain as taught by Tuse et al into the reagent components of Hashimoto et al because Hashimoto specifically taught that reagents for binding assays can be used to determine chitin in a sample and Tuse et al showed that immobilized chitin binding domain

reagents provide for detecting chitin in samples of all types of biological fluids and tissues and also provide the advantage of an efficient, economical, clinical laboratory assay reagents for the rapid diagnosis of fungal inflections in patients. It would have also been obvious to one of ordinary skill in the art at the time the invention was made to package the components of Tuse et al. and Hashimoto et al. into a kit format as taught by Foster because Tuse et al taught that it is known in the art to package components into a kit and further one or ordinary skill in the art would recognize that this would make it more convenient and facile for the test operator.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate instructions into the kit of Hashimoto et al as modified by Tuse et al. because Foster et al showed that instructions provide for the use of kit components and one skilled in the art would recognize that the addition of instructions would make it more convenient and facile for the test operator.

Response to Arguments

8. Applicant's arguments filed 06/10/09 have been fully considered but they are not persuasive.

Applicant argues that there is no suggestion or teaching in the Hashimoto et al reference of a method for detection of chitin in a sample also containing cellulose even though Hashimoto et al observe that CBD does not react with cellulose.

It is noted that even though it appears that Applicant is arguing that the sample of Hashimoto et al does not contain both chitin and cellulose, that Applicant provides a

table on page 14 of the amendment filed 06/10/09 that places a question mark within the table to question if the reference teaches that the sample contains both chitin and celluose. Regardless, the argument is not found persuasive because Hashimoto et al teaches that the binding assay mixtures comprise chitin and of the insoluble polysaccharides (e.g p. 3050 description of fig 5) and specifically that the chitin-binding domain bound only to chitin and that no significant binding to cellulose (polysaccharide) or other polysaccharides was detected (p. 3051, 2nd col). Therefore, absent evidence to the contrary it appears that the sample of Hashimoto et al contains both chitin and cellulose.

Applicant further argues that Hashimoto et al does not suggest that a chitin-binding domain (CBD) fused to maltose-binding domain (MBD) should be used for detection.

This is not found persuasive because the Examiner has not relied upon Hashimoto et al for such a teaching but rather has relied upon Chong et al for teaching that it is well know in the art to fuse CBD-MBP and Novokhatny teaches that the incorporation of maltose binding protein provides for purification of the target protein and as stated above, Hashimoto et al specifically teaches that the CBD can be produced in E-Coli. Additionally, Chong shows that it is well know in the art to fuse CBD-MBP and Novokhatny teaches that the incorporation of a carrier protein such as maltose binding protein provides for purification of the target protein. Therefore, for the reasons stated above the references provide the suggestion to have a CBD fused to MBD.

Applicant argues that the MBP of Chong et is not fused to CBD but rather is fused to an intein which is fused to CBD.

This is not found persuasive because the claim instantly recites "CBD fused to a maltose-binding domain". The claim does not recite if the CBD is directly fused or indirectly fused to the maltose-binding domain and as taught by Chong et al (e.g. 272) the maltose-binding protein was fused to the N-terminus of modified intein, and a chitin-binding domain.

Applicant argues that a person of ordinary skill in the art might refer to the Hashimoto et al. reference as a source of CBD for the described use of intein-mediated purification, but there is no teaching or motivation to construct the claimed method.

This is not found persuasive because of reasons stated above directed to the combination of Hashimoto et al., Chong et al and Novokhatny et al and further the instant claims do not specifically recite the relationship of the CBD in the method other than that the CBD binds the chitin. The claim does not exclude purification steps nor does the claim state if the CBD is directly labeled with a reporter or is indirectly detected to determine if binding has occurred.

Applicant argues that Novokhatny et al does not suggest or teach a method for detection of chitin in a sample also containing cellulose.

This is not found persuasive because applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case the Examiner has not relied upon Novokhatny for teaching the detection of chitin in a sample also containing cellulose but rather has relied upon Hashimoto et al for teaching this limitation (see rejections and arguments supra).

Applicant argues that the present claims are not directed to a method of purification of a target protein but that the present claims are directed to detection of a contaminant (chitin) in a sample also containing cellulose.

This is not found persuasive because of reasons stated above that the claims do not specifically recite the relationship of the CBD in the method other than that the CBD binds the chitin. The claim does not exclude purification steps nor does the claim state if the CBD is directed labeled with a reporter or is indirectly detected to determine if binding has occurred. Further, it is noted that there is noting recited in the claim that chitin is a contaminant.

Applicant argues that the Examiner has relied upon Gray et al for antibodies for detection and that the Hashimoto et al., Chong et al and Novokhatney et al references are not concerned with detection but rather describe methods of purification.

These arguments are not found persuasive because (1) the Examiner has not merely relied upon Gray for teaching antibodies for detection but also has relied upon Gray et al for teaching that it is known in the art to label chtin binding domains with a reporter to detect chitin in a sample and (2) Applicant's arguments that the references are not concerned with detection is completely off point. As stated above and in the previous office action Hashimoto et al specifically teaches detection.

Applicant further argues that the addition by the Examiner of the Gray et al reference to the combination of references is the result of hindsight based on Applicants claimed invention.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case Gray et al teaches that it is known in the art to utilize specific reagents for detection of chitin and it is within the level of ordinary skill at the time the claimed invention was made to incorporate reporters and antibodies such as taught by Gray et al into the modified method of Hashimoto et al for the detection of chitin.

Applicant argues that Tuse et al does not suggest or teach a method for detection of chitin in a sample also containing cellulose.

This is not found persuasive because applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case the Examiner has not relied upon Tuse for teaching the detection of chitin in a sample also containing cellulose but rather has relied upon Hashimoto et al for teaching this limitation (see rejections and arguments supra).

Applicant further argues that Tuse et al arguably contradict Hashimoto et al because Tuse et al utilize intact chitinase to "deduce the presence of chitin containing organisms in samples of all types of biological tissues and that Hashimoto et al state that "...chitinase AI exhibited weak but significant binding to cellulose in addition to various forms of insoluble chitin (p. 3051). Applicant states that cross reactions would invalidate the approach described by Tuse.

This is not found persuasive because the Examiner has not relied upon Tuse for methods but rather has relied upon Tuse for teaching that it is known in the art that chitin binding domains can be immobilized and used in methods of detection. In the instant case the Examiner has relied upon the primary reference of Hashimoto for teaching the detection utilizing the chitin-binding domain $CHBD_{ChiA}$ which is a different

binding domain than chitinase A1 which applicant is arguing. Further, as stated above the Examiner has relied upon Tuse for teaching that it is known in the art that chitin binding domains can be immobilized and used in methods of detection.

Applicant argues that Foster et al does not suggest or teach a method for detection of chitin in a sample also containing cellulose.

This is not found persuasive because applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case the Examiner has not relied upon Foster for teaching the detection of chitin in a sample also containing cellulose but rather has relied upon Hashimoto et al for teaching this limitation (see rejections and arguments supra). Applicant further argues that it appears that the Foster et al reference has little relevance to the claimed subject matter. This is not found persuasive because Foster teaches that it is very well known in the art to package components and instructions into a kit and as stated above one or ordinary skill in the art would recognize that this would make it more convenient and facile for the test operator. Thus, the reference is very relevant to teaching packaging components and instructions into a kit.

Applicant argues that Harman et al does not suggest or teach a method for detection of chitin in a sample also containing cellulose.

This is not found persuasive because applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case the Examiner has not relied upon Harman for teaching the detection of chitin in a sample also containing cellulose but rather has relied upon Hashimoto et al for teaching this limitation (see rejections and arguments supra).

Conclusion

9. No claims are allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GARY W. COUNTS whose telephone number is (571)272-0817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ Gary W. Counts/
Examiner, Art Unit 1641

/GAILENE R. GABEL/
Primary Examiner, Art Unit 1641 8/15/09